

Special article

Toxic mold: phantom risk vs science

Jean A. Chapman, MD*; Abba I. Terr, MD†; Robert L. Jacobs, MD‡; Ernest N. Charlesworth, MD§; and Emil J. Bardana, Jr, MD¶

Objective: To review the available literature on the subject of fungi (molds) and their potential impact on health and to segregate information that has scientific validity from information that is yet unproved and controversial.

Data Sources: This review represents a synthesis of the available literature in this area with the authors' collective experience with many patients presenting with complaints of mold-related illness.

Study Selection: Pertinent scientific investigation on toxic mold issues and previously published reviews on this and related subjects that met the educational objectives were critically reviewed.

Results: Indoor mold growth is variable, and its discovery in a building does not necessarily mean occupants have been exposed. Human response to fungal antigens may induce IgE or IgG antibodies that connote prior exposure but not necessarily a symptomatic state. Mold-related disease has been discussed in the framework of noncontroversial and controversial disorders.

Conclusions: When mold-related symptoms occur, they are likely the result of transient irritation, allergy, or infection. Building-related illness due to mycotoxicosis has never been proved in the medical literature. Prompt remediation of water-damaged material and infrastructure repair should be the primary response to fungal contamination in buildings.

Ann Allergy Asthma Immunol. 2003;91:222-232.

INTRODUCTION

After millions of years of benign existence, microscopic fungal spores are suddenly accused of causing problems. From stifling home sales to precipitating concerns about alleged health problems, mold has captured media headlines. Although fungi have been used for a multitude of purposes, ranging from the making of antimicrobial products to the making of cheese, they are now seen as a health concern and financial burden for homeowners, school districts, and tax payers.

In Texas, insurance companies were not concerned with mold-related problems until a homeowner in Dripping Springs was awarded a \$32 million settlement against Farmers Insurance Company in which the jury declared that the insurance company acted fraudulently and in bad faith when fixing water damage in a 22-room mansion by delaying the repair of a relatively small water leak.¹ The number of mold-related claims in Texas rose from 7,000 in the year 2000 to 37,000 in the year 2001. On June 9, 2001, tropical storm Allison poured rain onto the greater Houston area for 2 days, resulting in massive flooding along the Gulf Coast. In Houston alone, this resulted in a 58% increase in claims, which mushroomed to 2.96 claims for every 1,000 households insured.²

Like a train going at full steam, even celebrities have jumped on board. Entertainer Ed McMahon sued his insurance company for \$20 million in April 2002 for the death of his dog, allegedly from exposure to mycotoxins of *Stachybotrys chartarum*.¹ The new residence of basketball star Michael Jordan at the Ritz-Carlton in Washington, DC, is undergoing extensive renovations because of mold-related problems.¹ This hysteria does not just affect celebrities; tax payers in small and large towns alike remain concerned about the economic and health risks of mold exposure. Recent headlines such as "Central Classrooms Closed Due to Mold" in the San Angelo, TX, *Standard-Time* and "Mold Inside Dorm Delays Move-in at UT-San Antonio" in the *Houston Chronicle* illustrate the scope of this problem.^{3,4} The net effect of this response to fungal-related problems has been a staggering cost to the insurance industry, resulting in a loss of \$1.3 billion during this past year for removal and repair of mold-related damage and for settling lawsuits.¹ The response from the insurance industry has been simply to cut their losses by attempting to "get out of the business" of covering mold-related damages as illustrated by the recent decision of the nation's largest home insurer, State Farm Mutual Automobile Insurance Company, to eliminate coverage for mold related damages in 33 states.⁵

Medical science alone may not justify the public concern about mold, and one must wonder who is driving this train. Perhaps one answer might be found in an article written by Stephanie Francis Cahill, a staff journalist for the American Bar Association. In an article entitled "For Some Lawyers. Mold is Gold," she states that "toxic troubles translate into millions of dollars" and that "the practice area is growing

*Retired, Cape Girardeau, Missouri.

†University of California Medical Center, San Francisco, California.

‡Southwest Foundation for Biomedical Research, San Antonio, Texas.

§Uniformed Services University of the Health Sciences, San Angelo, Texas.

¶Division of Allergy and Immunology, Oregon Health and Science University, Portland, Oregon.

Received for publication December 31, 2002.

Accepted for publication in revised form March 17, 2003.

rapidly."⁶ She further adds, "in the past decade, attorneys have won millions of dollars in toxic mold verdicts in Texas, Delaware and California." She goes on to note that claims for asbestos are fading into memory but that "with mold, it's naturally occurring and the supply is endless ... claims involving adult onset asthma or cognitive functions such as short-term memory loss can be lucrative."

The purposes of this article are to objectively examine the legitimate issues of concern, review the scientific literature, and conclude with a statement founded on evidence-based science. Pertinent scientific investigation on toxic mold issues and previously published reviews on this and related subjects that met the educational objectives were critically reviewed. This review represents a synthesis of the available literature in this area with the authors' collective experience with many patients presenting with complaints of mold-related illness.

ECOLOGY OF THE MOLDS

Biologic Characteristics of the Fungi

Humans have coexisted with fungi for millions of years. The fossil record suggests that fungi were present 559 million years ago and may have evolved even earlier. Thousands of different types are flourishing and absorb food from substances such as soil, wood, decaying organic matter, and living plants and other organisms.⁷ Their size ranges from tiny unicellular organisms invisible to the naked eye to some of the largest multicellular organisms. The latter were among the first fungi recognized because some of the larger fruiting structures, such as mushrooms, were large enough to be seen without a microscope. In Michigan, for example, the underground portion of an individual *Armillaria* mushroom extends more than 30 acres. Examples of fungi include toadstools, puffballs, truffles, yeasts, mildews, smuts, and rusts. Some of these organisms are among the longest-living organisms on earth (ie, some lichens, a living partnership of a fungus and an alga, are thought to be more than 4,500 years old).⁷

The fungi are ubiquitous on earth and play an important role in the natural recycling process of decomposing organic matter into its constituent chemical components. They comprise approximately 25% of the earth's biomass, and their value to humankind is immeasurable.⁸ Some experts estimate there are 1.5 million fungus species, of which 100,000 have been specifically identified. Fewer than 100 are known to be primary pathogens (infectious agents) of humans and animals. The remainder are saprobic.⁹

Fungi require a continuous source of water, oxygen, and organic material and a suitable temperature for growth and development. They lack chlorophyll, the pigment that allows plants to make their own food. Fungi obtain nutriment by releasing digestive enzymes that break down food outside their bodies. They then absorb the dissolved food through their cell walls, which contain chitin, the same material that forms the exoskeleton of insects. Most fungi exist as filaments composed of long chains of cells. A few are unicellu-

lar, including the yeasts. Yeast are single-celled organisms that reproduce by budding. As a result, yeasts produce circular pasty or mucoid colonies. Most fungi, including the molds, are multicelled, filamentous forms that consist of thread-like strands of cells termed *hyphae* that interweave to form a mycelium. The resulting colonies are generally fuzzy. Most fungi reproduce by spores that are designed for airborne dispersal. The latter differ in number of cells, size, shape, and color.⁹ Their size may range from less than 2 μm to more than 100 μm . Spores are produced in mass. For example, one giant puffball produces an estimated 7 trillion spores.⁷

AIRBORNE LEVELS OF INDOOR FUNGI

Of all the bioaerosols worldwide, mold spores appear to constitute the largest portion in both indoor and outdoor environments.¹⁰ Under usual atmospheric conditions, concentrations of more than 100,000 spores/ m^3 are not exceptional.¹¹ Outdoor concentrations of fungal spores can vary widely by geographic location and even within a geographic location and significantly vary depending on seasonal climatic factors, including temperature changes, precipitation, humidity, prevailing winds, circadian patterns of darkness and sunlight, time of day, and degree of moisture.¹⁰⁻¹³ Spore types that are commonly found outdoors include *Basidiospores*, *Cladosporium*, *Ascospores*, *Alternaria*, *Penicillium*, and *Aspergillus*. However, the range of species found outdoors can be enormous and entirely dependent on the effort made to identify them. The most common indoor fungal species are *Cladosporium*, *Penicillium*, *Aspergillus*, *Alternaria*, and *Aureobasidium*.

Levels of airborne indoor fungi will generally be a reflection of outdoor sources. Indoor levels are usually 40% to 80% of outdoor levels, with similar species rankings, except when outdoor levels are low. However, a number of indoor activities and materials can also contribute to indoor mold sources, such as plants, pets, and molds brought in on footwear and clothing. Contaminated air conditioners and humidifiers can also circulate indoor spores and their allergens.¹¹ In addition, inadequate ventilation can add to the increased burden of fungal growth in the home. It has long been known that environmental conditions, such as temperature and humidity, promote the growth of both indoor mold and house-dust mite. Molds also serve as nourishment for the *Dermatophagoides* species, promoting their growth and survival.^{11,14,15} The latter becomes important in the attribution of any clinical symptoms that arise in the indoor setting.

MEASUREMENT OF INDOOR FUNGI

Fungal spores that are produced outdoors become widely dispersed and consequently can access most homes. For most genera, the highest numbers of fungi in the outdoor air are found during summer and autumn.¹⁶ Mechanical ventilation and air conditioning may modify this access by permitting windows to remain closed but may also become harbingers of mold growth if not properly maintained. Since outdoor levels can vary substantially in a short interval of time (ie, minutes or hours), comparisons with indoor concentrations during

similar periods have inherent pitfalls.^{11,17} This issue is magnified when dealing with relatively low concentrations of fungi measured by a small number of samples. In many assessments of airborne concentrations of indoor fungi, only 1 or 2 outdoor samples are collected. It is rare that one or more noncomplaint control homes are simultaneously checked to provide an expected baseline for the geographic area and season of the year.

Indoor sampling for fungi is affected by variables too numerous to detail in this brief review. There is no currently standardized collecting method that combines continuous volumetric sampling with reliable and complete identification of all fungal types.^{11,17} Therefore, depending on the type of technique used, reports on atmospheric fungal spores always give incomplete information. Nearly all indoor environments will contain some fungi. When assessing indoor air sampling data, one should have a comparable number of samples taken from proximal outdoor sites against which one can compare to indoor sampling.

Sometimes bulk or surface samples are collected rather than air samples. Concentrations of fungi detected in bulk samples of building materials that are not directly exposed to indoor ambient air (eg, space between siding and sheet rock, insulation material, wallboard) are not necessarily indicative of what inhabitants may be breathing. In postulating exposure, a reasonable pathway to the breathing zone of the occupant must be apparent. It has been estimated that 70% of homes have mold growing inside the walls. Some fungal spores require only movement of air for dispersal (eg, *Penicillium* and *Aspergillus*). Other species, such as *S. chartarum*, require some mechanical disturbance, such as water, animals brushing against the growth, or renovation or building activities.

Sampling approaches are not standardized, but the interpretation of the significance of any sampling data are even more problematic. There are also no uniform numeric standards for indoor airborne or surface fungi. There are more than 20 suggested guidelines. There is no consistent uniformity in these suggested guidelines¹⁸ and more importantly no uniform agreement or scientific support to sustain any given level of CFU/m³ as acceptable for human health. These guidelines have been published on the basis of consensus only.

Even more important is the fact that there is no known dose-response relationship between a specific ambient fungal concentration and any human health effects.¹⁹ Above all, since fungi are continuously encountered both indoors and outdoors, there is generally no way to ascribe any adverse health effect to any specific indoor exposure.

Several recent reviews concluded that average concentrations of fungi in indoor ambient air varies seasonally and geographically.^{20,21} For 85 homes with airborne concentrations reported as total spore counts, the average ranged from 68 to 2,307 spores/m³ for the indoor air and 400 to 80,000 spores/m³ in outdoor ambient air.²⁰ Gots et al²¹ found that ambient air in 820 residences without any health complaints averaged 1,252 CFU/m³, and the associated average outdoor level was 1,524 CFU/m³.

AIRBORNE CONCENTRATIONS OF FUNGI IN WORK SETTINGS

One reason for doubt about the role of indoor fungi in many reported symptom clusters is the absence of scientific evidence for adverse health effects in occupational settings with extremely high ambient concentrations of fungi. In sawmills, airborne concentrations have been reported as high as 1,500,000 CFU/m³.²² A study of differences in air concentrations on farms with and without adverse health effects revealed an average exposure concentration of 120,000,000 spores/m³ in the control farms where there were no complaints.²³ Daily spore levels associated with adverse health effects were at least 10 times greater (ie, 1,200,000,000 spores/m³). Indoor concentrations in spawning sheds on mushroom farms have been reported as high as 100,000 spores/m³.²⁴ Commercial composting activities have yielded airborne concentrations of more than 8,000,000 spores/m³. As in commercial and residential dwellings, there are no standards for airborne concentrations of fungi in the occupational setting. Although there are occasional reports of hypersensitivity pneumonitis in these work facilities, there are no reports of "brain damage" or other nonspecific mold-related disorders that are currently being alleged in indoor environments with comparatively modest airborne levels.

NONCONTROVERSIAL DISEASES CAUSED BY MOLD

There are 3 noncontroversial categories of disease caused by fungi: infection, allergy, and ingestion toxicity. All 3 have clearly identified, well recognized, objective clinical and pathologic effects that can be shown by physical examination, laboratory testing, and microscopic tissue examination. They are not merely subjective (ie, symptomatic only). Furthermore, allergy, infection, and ingestion toxicity are each specific to particular fungal species.

Allergy to Fungi

Mold allergy affects only a portion of the population. It usually leads to asthma but is not believed to be a common cause of allergic rhinitis. Rarely, fungal exposure produces hypersensitivity pneumonitis.

Atopy

Atopy is a symptom complex that consists of asthma, allergic rhinitis, atopic dermatitis, and allergic gastroenteropathy. These 4 diseases are mediated by IgE antibodies, although the manifestations need not be present in the same patient. There is a clear but complex genetic predisposition. The environmental allergen reacts with specific IgE antibodies that occupy receptor sites on the mast cell or basophil, thereby releasing or activating mediators of inflammation on the target organ.

Sensitization to fungi in atopic allergic disease was first recognized more than 70 years ago. Allergens from spores, mycelia, and other fungal particles may induce IgE antibodies. Individual fungal species may produce up to 40 distinct allergens, although cross-reactivity among species is com-

mon. Atopic disease caused by airborne fungi is almost exclusively confined to atopic asthma. Other dominant inhaled allergens are pollens, house-dust mite, and animal dander, and these more common allergies often accompany mold allergy within the same patient.

The diagnosis of mold allergy requires the demonstration of IgE antibody to relevant allergens by skin testing or in vitro tests using methods such as the radioallergosorbent test, but only in the context of a compatible history.

Nonatopic diseases, also mediated by IgE antibodies, are urticaria, angioedema, and anaphylaxis. The mechanism of disease is the same as in atopy, except that the target organ is the dermal vasculature or the systemic circulation, and there is no known genetic predisposition. The relevant allergens are primarily foods and drugs. Mold allergens are not recognized as a cause of these diseases except for anaphylaxis due to subcutaneous injections of fungal antigens given for immunotherapy.²⁵

Hypersensitivity pneumonitis (HSP), also known as extrinsic allergic alveolitis, is a chronic disease of the peripheral airways and interstitium, which may progress to pulmonary fibrosis. It is an allergic disease caused by inhalation of allergen on airborne organic particles. Most reported cases are occupational, but there are reports of HSP as a result of home contamination. Most of these reports are based on single case reports. Fungal spores have been implicated in a few cases, usually as part of a mixed aerosol with bacteria and other microorganisms.

The disease exists in 3 overlapping stages with characteristic pathologic features. The acute stage features a mononuclear cell pneumonitis, the subacute phase is characterized by an interstitial granulomatous inflammation, and the chronic phase is characterized by interstitial fibrosis. Both sensitization and elicitation of the disease require inhalation of large quantities of an organic antigen. The immunopathogenesis is a pan-immune response that involves both local and systemic sensitization. The cellular response is of primary importance in the pathogenesis of all forms of this disease. The humoral response, which involves all immunoglobulin isotypes, may be pathogenetic in the acute phase. An intense IgG antibody response detectable by precipitating antibodies may be useful to identify the causative antigen, but they are not disease specific.

Acute farmer's lung, a form of HSP, shares many clinical features with organic dust toxic syndrome (ODTS), such as chills, malaise, myalgia, dry cough, dyspnea, headache, and nausea after a heavy organic dust inhalation exposure. However, ODTS differs from acute HSP in several respects. The chest x-ray film does not show infiltrates, hypoxemia does not occur, previous sensitization to antigens in the organic dust is not required, and there are no significant sequelae, such as the recurrent attacks and the pulmonary fibrosis that may be seen with chronic HSP. ODTS is thought to be caused by endotoxin inhalation (ie, a toxic, not allergic, disease) and is much more common than farmer's lung.²⁶

Allergic bronchopulmonary aspergillosis (ABPA) is a complication in some patients with atopic asthma or cystic fibrosis. *Aspergillus fumigatus* spores are trapped in thick bronchial mucus, leading to specific IgE and IgG antibodies and T-cell sensitization. The most common allergen is Asp f 1, which is produced within the mycelium only after spore germination. The disease is a noninfectious, immunologic bronchial inflammation. Symptoms are cough, wheezing, sputum, fever, weight loss, pulmonary infiltrates, and mucous plug expectoration. The course is one of remissions and exacerbations, resulting in progressive central bronchiectasis and interstitial fibrosis, deteriorating pulmonary function, which is potentially fatal.

The minimal essential criteria for the diagnosis of ABPA are as follows: (1) asthma, (2) central bronchiectasis, (3) total serum IgE level of more than 1,000 ng/mL, (4) a positive wheal-and-flare skin test result to *A. fumigatus*, and (5) serum IgE and/or IgG antibodies to *Aspergillus*. Other features that may be present are a sputum culture for *A. fumigatus*, expectoration of mucous plugs containing the organism, a positive Arthus skin test result to *A. fumigatus*, and a decline in serum IgE level with prednisone therapy. Other fungi may also be involved.

Allergic Fungal Rhinosinusitis

Allergic fungal rhinosinusitis was first described in 1976, but the definition and diagnosis of the condition have not yet been clearly established. The prevalence and the specific fungi that cause the disease vary geographically. Dematiaceous fungi, such as *A. fumigatus* (which may accompany ABPA) and *Bipolaris spicifera*, are commonly involved, especially found in the southwestern United States. The clinical presentation is typically described as one of recurrent hypertrophic sinusitis in an atopic patient. The fungus may be cultured from nasal or sinus mucus, and there is a positive wheal-and-flare skin test result to the organism. Nasal polyposis is common, total serum IgE level may be elevated, eosinophils and lymphocytes are present in mucosal inflammation (allergic mucin), and hyphae are occasionally found in the inspissated mucus. Recurrences are common despite surgery and systemic glucocorticoids. Thus, the disease has features of both infection and allergy. Neither ABPA nor allergic fungal rhinosinusitis has been associated with specific indoor exposure to fungi.

Infection with Fungal Toxins

Fungal infections may be localized to the skin and mucous membranes, or they may be systemic. In either of these forms, infection may occur environmentally in certain locations that breed pathogenic fungi. The more common infectious fungi are those that cause histoplasmosis, coccidioidomycosis, blastomycosis, paracoccidioidomycosis, sporotrichosis, and penicilliosis. *Actinomyces* (*Nocardia*, *Actinomyces*), which are bacteria with morphologic characters in common with fungi, may also cause infection.

Opportunistic infections occur in immunosuppressed patients (eg, in patients with acquired immunodeficiency syndrome,²⁷ patients with cancer,²⁸ or patients taking immunosuppressant drugs). They also occur in patients with diabetes, alcoholism, and neutropenia and those receiving broad-spectrum antibiotics or corticosteroids. The fungi that commonly cause infections under these conditions are *Candida*, *Cryptococcus*, *Aspergillus*, *Fusarium*, and *Mucor*. Many more rare examples exist, each specific to a particular fungus.²⁹ Fungal infections can be localized to unusual sites, such as the central nervous system, or disseminated with metastatic disease in any organ or serosal surface, bone, joints, tissue abscesses, and lymph nodes.

Fungi Toxins

All fungi, in common with other microorganisms, produce and liberate an array of chemicals that are necessary for their survival, nourishment, and propagation under a range of conditions, as well as many waste products or "secondary metabolites." The biosynthesis of these chemicals depends on and therefore varies with the age of the hyphae, available nutrients, and physical environment. Each chemical is termed a *toxin* when it can be shown to have a particular adverse physiologic effect on another living organism (animal, plant, or other microorganism) under appropriate conditions of exposure. Mycotoxins are a group of the secondary metabolites that share chemical structure characteristics. All have relatively low molecular weights (approximately 300 to 500 Da) and ring structures.

Toxic Effects Caused by Ingestion

Mushroom poisoning is a well recognized example of ingestion of a toxin produced by a mold. In the 1930s, horses in the Ukraine that were fed contaminated barley, corn, and wheat stored under winter snow developed alimentary bleeding, hemorrhage in other visceral organs, ulcerations, agranulocytosis, and death. Cases in humans that resulted from ingestion of grains contaminated with *Fusarium* and *Stachybotrys* were reported in Japan and Russia and referred to as "alimentary toxic aleukia." At the time of these observations and later, a similar disease occurred in some of the local farmers in contact with mold-contaminated hay or straw.

Mycotoxicosis is an important worldwide veterinary disease that affects other large farm animals as well, such as sheep, cows, swine, deer, and calves. The condition in animals typically follows a heavy rainfall and is often characterized by hemorrhage in other visceral organs. Since the 1940s, however, no additional human case reports or epidemics have been published, although it remains a threat to farm animals. In addition, elevated rates of some human cancers have been reported in developing countries related to ingestion of mycotoxins.

CONTROVERSIAL DISEASES OR CONDITIONS ATTRIBUTED TO MOLDS

Many controversial human case reports exist in which symptom complexes are alleged to involve *Stachybotrys* and other

fungi as the presumed cause of illness in water-damaged homes and office buildings. In some cases, *Cladosporium*, *Penicillium*, *Aspergillus*, and *Alternaria* species or combinations of them are invoked. Unlike the well recognized and noncontroversial disease states, these conditions are not specifically alleged to be caused by an individual mold species. Many of these patients report fatigue, cognitive difficulties, and problems with memory, and some are asymptomatic. They usually have no physical findings, pathologic features, or laboratory evidence of disease. There is no plausible pathogenic mechanism of disease. *S. chartarum* is the fungus most commonly implicated in nonspecific symptom complexes.

Infection

No human cases of infection caused by *Stachybotrys* have been reported to date.

Allergy

In 1980, Kozak et al³⁰ cited the case of a 4-year-old, asthmatic boy whose asthma improved when he was removed from his home. *Stachybotrys* was found in a water-damaged bedroom carpet but not in air samples. Although *Stachybotrys* allergy was suspected as the cause of his asthma, no allergy testing was reported.³⁰

Hypersensitivity Pneumonitis

There is no case of HSP caused by *Stachybotrys* in the published literature. Because an unusually high level of inhaled antigen is required in its pathogenesis, *Stachybotrys* as a cause of this disease would be most unlikely, considering the extremely low airborne levels of *Stachybotrys* spores in homes or buildings, even where there are obvious sources of the fungus identified on water-damaged surfaces. There are rare cases of HSP caused by other molds, usually identified as single case reports in an industrial setting in which the patient is exposed to extremely high concentrations of the specific allergen.

Toxicity by Inhalation

The first published report of disease alleged to be caused by inhalation of *Stachybotrys* spores appeared in 1986 in which 5 members of a family and their maid were subject to "recurring cold and flu symptoms, sore throats, diarrhea, headaches, fatigue, dermatitis, intermittent focal alopecia, and generalized malaise," even though the results of repeated medical examinations were negative for disease. *Stachybotrys atra* (*chartarum*) was cultured from air, and an undescribed "crude test" was said to show the presence of mycotoxin. An ethanol extract of *S. atra*—containing debris from an air duct was fatal when injected into weanling rats and adult mice, but there were no appropriate controls. The authors concluded nevertheless that the family illness was caused by airborne trichothecenes from *Stachybotrys*.³¹

Subsequently, epidemiologic studies have been performed on workers in several office buildings that had sustained water damage.^{32,33} Subjects were limited to those seen in an

damaged
sporium,
combina-
ized and
not spe-
species,
ficulties,
stomatic
features,
plausible
fungus
m com-

occupational health clinic or by volunteering and were not randomly selected. The diagnoses were obtained from a health complaint questionnaire, which elicited numerous specific and nonspecific symptoms. Physical examinations were not reported. Typically, the workers had numerous health complaints, especially neuropsychological and upper respiratory tract symptoms. Fungi, including *Stachybotrys*, were recovered on bulk samples of water-damaged materials, but only trace quantities of *Stachybotrys* spores, if any, were recovered from air samples. The investigators concluded that some workers had experienced an allergic or immunotoxic disease from "toxigenic" *S. atra* or other "atypical" fungi.

ys have

thmatic
om his
droom
allergy
testing

in the
of in-
rys as
dering
res in
ces of
re are
tified
h the
of the

A geographic cluster of 10 cases of acute pulmonary hemorrhage or hemosiderosis occurred among infants from 1 to 8 months of age living in a localized inner-city area of Cleveland, Ohio, between January 1993 and December 1994.³⁴ The disease was successfully treated in the hospital but recurred in 5 of the infants shortly after they returned home. One infant died. Based on epidemiologic evidence of severe water damage from flooding, resulting in fungal indoor growth in the homes of the patients, the illness was believed to be caused by mycotoxins from inhaled *Stachybotrys*. Environmental tobacco smoke was the only other risk factor identified in the infants' homes. Between 1993 and 1998, a total of 37 infants had been diagnosed as having idiopathic pulmonary hemorrhage in metropolitan Cleveland, with 12 deaths, including 7 originally diagnosed as sudden infant death syndrome. Thirty of these infants lived in a limited area of older housing, with water damage and household exposure to *S. atra* and other fungi. Because adults and older children in the household were unaffected, these investigators postulated that the rapidly growing lungs of young infants were vulnerable to the toxigenic mold, *S. atra* and the closely related fungus *Memnoniella echinata* recovered from these homes were believed to be responsible for these cases because of their potential to produce highly toxic trichothecene mycotoxins.³⁵

ed by
hich
"re-
ead-
and
ated
bot-
de-
/CO-
an
dult
ors
by

red
red
an

Although the Cleveland experience has been widely discussed and is responsible for an intense search for *Stachybotrys*-associated disease elsewhere, especially in homes and workplaces with water intrusion from roof or foundation leaks, 2 expert panels appointed by the US Centers for Disease Control and Prevention recently found serious flaws in the studies and concluded that the evidence for *Stachybotrys* as the cause of pulmonary hemorrhage in the infants was not proved. Specifically, sampling of cases and control homes differed and was not standardized; there was no case definition of the disease; some of the data were skewed by extremely high outlying values; and the diseases was not believed to be consistent with idiopathic pulmonary hemosiderosis because of the acute onset, limited age range, and absence of iron deficiency. There were concerns about quantitation of water damage and the clinical significance (vs contamination) of the exposure measurements of *Stachybotrys* or its toxins. It was concluded that "a possible association between acute pulmonary hemorrhage . . . and [mold] exposure . . . was not proven."³⁶

At least 100 cases of acute idiopathic pulmonary hemorrhage with or without hemosiderosis in which *Stachybotrys* was present within the home have been reported in infants in the United States during the past 5 years. In several cases, the organism was also recovered from the patient's lung.³⁷⁻³⁹ However, the presence of the organism is not proof of causality.

Toxic Effects by Contact

There is one report of fingertip skin inflammation in 3 women handling moldy horticulture pots contaminated with black masses of *Stachybotrys conidia*, *Chaetomium perithecia*, and other fungi. Painful inflamed efflorescences at the fingertips were described. Although a mycotoxin was postulated as the cause, no tests were performed to determine the etiologic agent or the mechanism (allergic or irritant contact dermatitis, toxicity, or infection). Surprisingly, these women handled pots that released up to 7,500 conidia per cubic meter of air, although none of them reported respiratory or systemic disease under these conditions.⁴⁰

NONSPECIFIC HEALTH EFFECTS OF HOME DAMPNES

Epidemiologic studies from several worldwide geographic locations have shown a significant difference between respiratory tract symptoms in children^{41,42} and adults^{43,44} living in damp homes and a similar population living in dry homes. Nafstad et al,⁴¹ in a case-control study of 251 cases of Norwegian children younger than 2 years with bronchial obstruction and their matched paired controls, found that dampness of the home increased the risk of bronchial obstruction independent of exposure to house dust mites.

Brunekreef et al⁴² studied 4,625 8- to 12-year-olds living in 6 US cities by questionnaire only and concluded that self-reported dampness in the home is a predictor of symptoms of the respiratory tract. Waegemaekers et al⁴³ studied 185 homes with 519 occupants in The Netherlands by questionnaire. In damp homes, respiratory symptoms were more prevalent in adults and children, whereas other health complaints were more prevalent in children. Culturable fungal measurements performed on 36 selected homes considered damp by the occupant had mean concentrations of 214 CFU/m³ compared with 91 CFU/m³ in dry homes. Dales et al⁴⁴ studied 14,800 adults from Canada by questionnaire only, concluding that exposure to home dampness and mold may be a risk factor for self-reported respiratory disease. Airborne mold concentrations were not measured.

Zock et al⁴⁵ found that self-reported mold exposure was associated with asthma symptoms and bronchial responsiveness in adults in 38 centers from the European Community Health Survey and was stronger in subjects sensitized to *Cladosporium*.

Sensitivity to other fungi and nonfungal allergens was not reported, and nonspecific factors related to dampness were not excluded. Several similar studies⁴⁶⁻⁴⁸ have shown a relationship between damp homes and respiratory tract symptoms. None of

these epidemiologic studies have been validated by actual measurements of humidity and airborne mold analyses.

PHYSICIAN EVALUATION

When confronted with a patient who has a clinical presentation that suggests that an indoor mold contamination may be playing a role in causing or aggravating a respiratory tract disorder, one must approach these evaluations with well defined methods to arrive at an appropriate decision. Table 1 details a practical approach to diagnosing a suspected building-related illness.⁴⁹

The history is the most important source of information during these evaluations.⁵⁰ Date of onset, worsening of symptoms, persistence of symptoms, improvement with long periods outside (up to 2 weeks), and exacerbation on return to the suspected environment are suggestive symptomatic clues. The home environmental history must be detailed, including information concerning odors, visible mold growth, roof and plumbing leaks, outside water, air conditioning problems, basement conditions, inside animals and birds, and general daily use pattern of the home (temperature settings, plants, use of humidifiers, vaporizers).⁵¹ Workplaces must be evaluated in the same detail as the home with considerations toward exposure to associated chemicals, dusts, fumes, and particulate matter. Medical history and review of systems may provide additional clues to discern the origin, including drugs, treatments, and other system complaints. A physical examination is unlikely to be helpful in determining if the disorder is environmentally induced or caused by other mechanisms, but it is essential to provide objective evidence of disease.

If a deep-seated mycosis is suspected, an infectious disease specialist should be consulted. Systemic fungal

infections of many types may occur in immunocompromised patients. Patients may develop tuberculosis, atypical mycobacterium infections, *Pneumocystis carinii* pneumonia, and other atypical pneumonias that may prove difficult to distinguish from hypersensitivity pneumonitis and idiopathic interstitial lung disease.⁵⁰⁻⁵²

Phenotyping the patient as atopic vs nonatopic gives insight as to the possible mechanism (allergic vs irritant). This may be helpful for long-term prognosis, since the atopic patient may continue to experience symptoms from outside exposure and the irritant-induced symptoms should resolve on remediation or moving from the environment. If the patient complains of lower respiratory tract symptoms, prebronchodilator and postbronchodilator spirometry is important to detect both obstructive and restrictive disorders. When the results of chest x-ray examination and computed tomography of the chest are abnormal, a pulmonary specialist and/or infectious disease specialist should be consulted regarding bronchoscopy, bronchial washings, and possible transbronchial biopsy. Supportive serologic testing, including total serum immunoglobulins, total IgE, rheumatoid factor, antinuclear antibody titer, sedimentation rate, C-reactive protein, and complete blood cell count with differential, is useful in defining the inflammatory and immunologic status of the patient. Screening serum precipitins as performed by standard commercial laboratories are of limited value.⁵⁰⁻⁵²

Environmental surveys can be performed by the patient, a family member, or a contractor and consist of 3 important components: smell, visualization, and culture collection and analysis of samples.^{51,52} The environmental history commonly gives strong clues as to where one should find a contamination.⁵¹

Table 1. Practical Approach to Diagnosing a Suspected Building-Related Illness

Evaluation	Components
Comprehensive medical history	Duration and nature of symptoms, home environment, workplace history, medical history, and family history
Physical examination	
Exclusion of more common infectious causes	Systemic fungal infections in immunocompromised patients, tuberculosis, atypical mycobacterium infections, and <i>Pneumocystis carinii</i> pneumonia
Determination of whether the patient is atopic vs nonatopic	Skin testing to seasonal and perennial allergens, mold panel, corresponding serologic testing, or prebronchodilator and postbronchodilator spirometry
Chest x-ray film or high-resolution computed tomogram of chest	Determine if pulmonary findings are consistent with hypersensitivity pneumonitis and require additional evaluation
Supportive testing, including serological testing for specific IgG, IgE, or IgA to fungi including <i>Stachybotrys</i>	Hypersensitivity pneumonitis screen (precipitating antibodies) and consideration of humoral and cell-mediated immune system evaluation
Environmental assessment	Walk-through observation, sampling to document exposure from suspect sources, and measurement by a qualified professional of known perennial allergens
Measurement of total symptom scores	In and out of the environment
Prebronchodilator and postbronchodilator measurement of spirometry	In and out of the putative home or workplace every 2-3 hours while awake and correlate with environmental exposure measurement

Environmental avoidance challenge techniques for nonspecific symptoms, chronic coughs, and asthma-like symptoms are difficult to establish cause-and-effect relationships due to a lack of objective measurements. Since the mechanisms of these complaints are probably allergic or irritant, only a short period (3 to 5 days) out of a causative environment is needed for symptoms to resolve or stabilize. On reentering the causative environment, symptoms recur usually within 24 hours. Environmental avoidance challenge techniques for patients with idiopathic interstitial lung disease or classic HSP are much easier procedures to perform because of objective markers. These procedures may confirm causative environment within 2 weeks in most cases.⁵³ Inhalational challenges to specific antigens are usually not necessary in the clinical setting. Determining the specific antigen may prove difficult because most contaminated environments have multiple fungi that would require multiple challenges. Knowing the specific cause does not alter the remediation attempts.

After remediation has been completed, the patient should remain at a precontamination baseline. Recurrence of symptoms implies ineffective remediation or an incorrect diagnosis, and further investigation may be necessary.

ASSESSMENT AND REMEDIATION OF FUNGI IN THE INDOOR ENVIRONMENT

Prompt remediation of contaminated material and infrastructure repair is the primary response to fungal contamination in buildings. Emphasis should be placed on preventing contamination through proper building and heating, ventilation, and air-conditioning (HVAC) system maintenance⁵⁴ and prompt repair of water damage.⁵⁵ Other specific detailed recommendations for residential and commercial properties are available.⁵⁴

Many fungi in addition to *S. chartarum* (eg, species of *Aspergillus*, *Penicillium*, *Fusarium*, *Trichoderma*, and *Memnoniella*) can produce potent mycotoxins. Many of these mycotoxins are shared among species, and they are identical to mycotoxins produced by *S. chartarum*. For this reason, *S. chartarum* cannot be treated as uniquely toxic in indoor environments.⁵⁵

Although there is evidence of a relationship both between very high levels of inhalation and direct contact with mycotoxin-containing fungi and adverse health effects, the current literature does not provide compelling evidence that exposures expected in most mold-contaminated indoor environments are likely to result in measurable health effects.⁵⁶ Research involving the identification and isolation of specific fungal toxins in the environment and in humans is needed before a more definitive link between health outcomes and mycotoxins can be made.⁵⁷

There are only a few articles that describe health effects both before and after remediation. For example, remediation efforts that addressed the contamination of the HVAC system involved the hiring of a dedicated mechanic to implement a HVAC preventive maintenance program that included the regular replacement of all HVAC air filters and the cleaning

of accessible components with a water and bleach solution, resulting in the resolution of the "sick building syndrome" in a high-security facility.⁵⁸ In another example, in a new building in which visible fungal growth was present and in which an outbreak of allergic respiratory disease existed, all visibly colonized materials were discarded and all fine dust on interior surfaces was removed by vacuuming and damp wiping to clean the contaminated area.⁵⁹ The literature concerning cleanup and remediation needs to be further developed, since much of what is recommended is empiric and not based on scientific studies. The contentious issues relate to how extensive the cleanup should be.

Environmental Assessment

A visual inspection is the most important initial step in identifying a possible contamination problem. The extent of any water damage and mold growth is determined by the visual inspection and will help to determine the remedial strategies.⁵⁵ The investigation should include an inspection of the HVAC system, particularly damp filters, but also an examination for damp conditions that exist elsewhere in the system and an examination for overall cleanliness.⁵⁵ Ceiling tiles, gypsum wallboard (sheet rock), paper, and other cellulose-containing surfaces should be given special attention.

There are no widely accepted quantitative standards or guidelines for the presence of fungi in indoor air. Published standards are determined by baseline data (rather than health effects data). These data are numerical comparisons, indoor-outdoor comparisons, or a combination of both. Quantitative standards and guidelines range upward from less than 100 CFU/m³ (total fungi) as the upper limits for noncontaminated indoor environments. Major concerns with the existing quantitative standards and guidelines are the lack of any connection to human dose-response data, reliance on short-term grab samples that are analyzed only by culture, and the absence of standardized protocols for data collection, analysis, and interpretation.¹⁸

Remediation

The presence of mold, water damage, or musty odors should be addressed immediately. In each instance, any source of water incursions should be stopped and the extent of water damage determined. Water-damaged materials should be dried and repaired or discarded.⁵⁵

The essential step is to remove water from the environment.⁶⁰ In all situations, the underlying cause of the water accumulation should be corrected or fungal growth will recur. Any initial water incursion should be stopped and cleaned immediately. An immediate response (within 24 to 48 hours) and thorough cleanup, drying, and/or removal of water-damaged materials will prevent or limit mold growth. If the source of water is elevated humidity, leading to condensation, then relative humidity should be maintained at levels below 60% to inhibit mold growth.⁶¹

The New York City Department of Health has issued suggested guidelines for the evaluation and the remediation

of fungi in indoor environments.⁵⁵ These guidelines divide abatement into 4 different levels, ranging from small isolated areas of 10 sq ft or less to more extensive contamination with greater than 100 contiguous sq ft in an area with specific recommendations. In addition, the HVAC systems are considered for abatement based on less than 10 sq ft to greater than 10 sq ft, again with specific recommendations relevant to the size of the area of contamination. The use of gaseous ozone or chloride dioxide for remedial purposes is not recommended.⁵⁵

For the people performing renovations and cleaning of widespread fungal contamination, proper protection is recommended, such as a N95 disposable respirator, gloves, and eye protection.^{53,62} For large areas of fungal contamination, a health and safety professional with experience performing microbial investigations should be consulted before undertaking remediation to provide oversight for the project. The reader is referred to the following resources on the World Wide Web for more detailed information and recommendations regarding the evaluation and remediation of the indoor environment:

1. US Environmental Protection Agency. Indoor air—mold/moisture. In: *Mold Resources: A Brief Guide on Mold, Moisture and Your Home: Mold Remediation in Schools and Commercial Buildings*.
2. Occupational Safety and Health Administration, US Department of Labor. Indoor air quality investigation. In: *OSHA Technical Manual*. Section III, chap 2.
3. American Conference of Governmental Industrial Hygienists Inc. Janet Macher, editor. *Bioaerosols: Assessment and Control*. ISBN: 1-882417-29-1. 1999, 322 pages.

RECOMMENDATIONS

The allergist/clinical immunologist is frequently consulted to evaluate a purported mold-contaminated home, school, or workplace and evaluate potential causation of adverse health effects. Accordingly, as allergists and immunologists we need to be familiar with the current science of mold-related illnesses. We encourage physicians and involved health care personnel to familiarize themselves with the literature on this subject. It is in our patients' best interest to use common sense in assessing patient complaints and in investigating suspect indoor environments. We advocate evaluating patients and their environment in a practical and uniform way, which has been outlined in this review.

To better counsel patients, privately sponsored and industry-sponsored research needs to be performed to better define the potential for toxicity and define minimal exposure levels involved in human disease. At this point, there is little science to support the public concern and to justify the prodigious number of lawsuits. In many respects, this area remains a "black box" in which there is little science to support the public reaction.

ACKNOWLEDGMENT

The authors thank Ms. Mary Lou Callaghan for her valuable assistance with this article.

REFERENCES

1. Sharpe R. Mold getting a costly hold on homes. *USA Today*. June 19, 2002.
2. Montemayor J, commissioner, Texas Department of Insurance. Mold Data Territory Summary: Moderate-Large Claims Only (>\$4,999). September 18, 2001. Available at: www.tdi.tx.us/commish/molddata.
3. Wintermantel, Gretchen M. Central classrooms closed due to mold. *San Angelo Standard-Times*. May 14, 2002.
4. Associated Press. Mold inside dorm delays move-in at UT-San Antonio. *Houston Chronicle*. August 26, 2002.
5. Oster C. Insurance companies just say "no" to covering mold. *Wall Street Journal*. August 8, 2002.
6. Cahill SF. For some lawyers, mold is gold. *Am Bar Assoc J*. December 2001.
7. Fungus. In: *Microsoft Encarta Online Encyclopedia 2002*. Available at: <http://encarta.msn.com>. Accessed January 25, 2003.
8. Miller JD. Fungi as contaminants in indoor air. *Atmospheric Environ*. 1992;26A:2163-2172.
9. Dixon DM, Fromtling RA. Morphology, taxonomy, and classification of the fungi. In: Murray PR, editor-in-chief. *Manual of Clinical Microbiology*. 6th ed. Washington, DC: ASM Press; 1996:699-708.
10. D'Amato G, Spieksma FT. Aerobiologic and clinical aspects of mold allergy in Europe. *Allergy*. 1995;50:870-877.
11. Reynolds SJ, Streifel AJ, McJilton CE. Elevated airborne concentrations of fungi in residential and office environments. *Am Ind Hyg Assoc J*. 1990;51:601-604.
12. Solomon WR. Assessing fungus prevalence in domestic interiors. *J Allergy Clin Immunol*. 1975;56:235-242.
13. Burge H, ed. *Guidelines for the Assessment of Bioaerosols in the Indoor Environment*. Cincinnati, OH: American Conference of Governmental Industrial Hygienists; 1989:108-109.
14. Beguin H. Mold biodiversity in homes, II: analysis of mattress dust. *Aerobiologia*. 1995;11:3-10.
15. Van Bronswijk JE, Sinha RN. Role of fungi in the survival of *Dermatophagoides* in housedust environment. *Environ Entomol*. 1973;2:142-145.
16. Verhoeff AP, van Wijnen JH, Brunekreef B, Fischer P, van Reenen-Hoekstra ES, Samson RA. The presence of viable mold propagules in indoor air in relation to home dampness and outdoor air. *Allergy*. 1992;47:83-91.
17. Horner WE, Lehrer SB, Salvaggio JE. Fungi. *Immunol Allergy Clin North Am*. 1994;14:551-565.
18. Rao CY, Burge HA, Chang J. Review of quantitative standards and guidelines for fungi in indoor air. *J Air Waste Manag Assoc*. 1996;46:899-908.
19. Fung F, Hughson WG. Health effects of indoor fungal bioaerosol exposure. *Proc Indoor Air*. 2002;3:46-51.
20. Shelton BG, Kirkland KH, Flanders WD, Morris GK. Profiles of airborne fungi in building and outdoor air environments in the United States. *Appl Environ Microbiol*. 2002;68:1743-1753.
21. Gots RE, Layton N, Pirages SW. Indoor health: background levels of fungi. *Am Ind Hyg Assoc J*. In press.
22. Duchaine C, Meriaux A, Thorne PS, Coumier Y. Assessment of

valuable

4 Today

insurance,
ms Only
tdi.tx.us

1 due to

UT-Sun

g mold.

Assoc. J.

2012,
ary 25,

spheric

classi-
fical of
Press;

ects of

e con-
ts. Am

interi-

ols in
tence

utress

val of
Ento-

, van
mold
and

lergy

iards
ssoc.

ero-

files
s in
753.
und

it of

- particulates and bioaerosols in eastern Canadian sawmills. *Am Ind Hyg Assoc J.* 2000;61:727-732.
23. Malmberg P, Rask-Andersen A, Rosenhall L. Exposure to microorganisms associated with allergic alveolitis afebrile reactions mild dust in farmers. *Chest.* 1993;103:1202-1209.
24. Lacey J, Crook B. Fungal and actinomycete spores as pollutants of the workplace and occupational allergens. *Ann Occup Hyg.* 1988;32:515-533.
25. Ostergaard PA, Kaad PH, Kristensen T. A prospective study on the safety of immunotherapy in children with severe asthma. *Allergy.* 1986;41:588-593.
26. Von Essen S, Robbins RA, Thompson AB, Rennard SI. Organic dust toxic syndrome: an acute febrile reaction to organic dust exposure distinct from hypersensitivity pneumonitis. *Clin Toxicol.* 1990;28:389-420.
27. Walsh TJ, Groll AH. Emerging fungal pathogens: evolving challenges to immunocompromised patients for the twenty-first century. *Transpl Infect Dis.* 1999;1:247-261.
28. Anissie E, Kantarjian H, Ro J, et al. The emerging role of *Fusarium* in patients with cancer. *Medicine.* 1988;67:77-83.
29. Hilmarssondottir I, Meynard JL, Rogeaux O, et al. Disseminated *Penicillium marneffei* infection associated with human immunodeficiency virus: a report of two cases and review of 35 published cases. *J Acquir Immune Defic Syndr.* 1993;6:466-471.
30. Kozak PP Jr, Gallup J, Cummins LH, Gillman SA. Currently available methods for home mold surveys, II: examples of problem homes surveyed. *Ann Allergy.* 1980;45:167-76.
31. Croft WA, Jarvis BC, Yatawara CS. Airborne outbreak of trichothecene toxicosis. *Atmospheric Environ.* 1986;20:549-552.
32. Johanning E, Biagini R, Hull D, Morey P, Jarvis B, Landsbergis P. Health and immunology study following exposure to toxigenic fungi (*Stachybotrys chartarum*) in a water-damaged office environment. *Int Arch Occup Environ Health.* 1996;68:207-218.
33. Hodgson MJ, Morey P, Leung WY, et al. Building-associated pulmonary disease from exposure to *Stachybotrys chartarum* and *Aspergillus versicolor*. *J Occup Environ Med.* 1998;40:241-249.
34. Etzel RA, Montana E, Sorenson WG, et al. Acute pulmonary hemorrhage in infants associated with exposure to *Stachybotrys atra* and other fungi. *Arch Pediatr Adolesc Med.* 1998;152:757-762.
35. Dearborn DG, Yike I, Sorenson WG, Miller MJ, Etzel RA. Overview of investigations into pulmonary hemorrhage among infants in Cleveland, Ohio. *Environ Health Perspect.* 1999;107(Suppl):495-499.
36. Centers for Disease Control and Prevention. Update: pulmonary hemorrhage/hemosiderosis among infants—Cleveland, Ohio, 1993-1996. *JAMA.* 2000;283:1951-1953.
37. Elidemir O, Colasurdo GN, Rossmann SN, Fan LL. Isolation of *Stachybotrys* from the lung of a child with pulmonary hemosiderosis. *Pediatrics.* 1999;104:964-966.
38. Knapp JF, Michael JG, Hegenbarth MA, Jones PE, Black PG. Case records of the Children's Mercy Hospital, case 02-1999: a 1-month-old infant with respiratory distress and shock [clinical conference]. *Pediatr Emerg Care.* 1999;15:288-293.
39. Vesper SJ, Dearborn DG, Elidemir O, Haugland RA. Quantification of siderophore and hemolysin from *Stachybotrys chartarum* strains, including a strain isolated from the lung of a child with pulmonary hemorrhage and hemosiderosis. *Appl Environ Microbiol.* 2000;66:2678-2681.
40. Dill I, Trautmann C, Szewzyk R. Mass development of *Stachybotrys chartarum* on compostable plant pots made from recycled paper. *Mycoses.* 1997;40(Suppl):110-114.
41. Nafstad P, Oie L, Mehl R, et al. Residential dampness problems and symptoms and signs of bronchial obstruction in young Norwegian children. *Am J Respir Crit Care Med.* 1998;157:410-414.
42. Brunekreef B, Dockery DW, Speizer FE, et al. Home dampness and respiratory morbidity in children. *Am Rev Respir Dis.* 1989;140:1363-1367.
43. Waegemackers M, van Wageningen N, Brunekreef B, et al. Respiratory symptoms in damp homes. *Allergy.* 1989;44:192-198.
44. Dales RE, Burnett R, Zwanenburg H. Adverse health effects among adults exposed to home dampness and molds. *Am Rev Respir Dis.* 1991;143:505-509.
45. Zock JP, Jarvis D, Luczynska C, et al. Housing characteristics, reported mold exposure, and asthma in the European Community Respiratory Health Survey. *J Allergy Clin Immunol.* 2002;110:285-292.
46. Jaakkola MS, Nordman H, Piipari R, et al. Indoor dampness and molds and development of adult-onset asthma: a population-based incident case-controlled study. *Environ Health Perspect.* 2002;110:543-547.
47. Williamson U, Martin CJ, McGill G, et al. Damp housing and asthma: a case-control study. *Thorax.* 1997;52:229-234.
48. Andriessen JW, Brunekreef B, Roemer W. Home dampness and respiratory health status in European children. *Clin Exp Allergy.* 1998;28:1191-1200.
49. Trout D, Bernstein J, Martinez K, et al. Bioaerosol lung damage in a worker with repeated exposure to fungi in a water-damaged building. *Environ Health Perspect.* 2001;109:641-644.
50. Patterson R, Greenberger PA, Castile RG, et al. Diagnostic problems in hypersensitivity lung disease. *Allergy Proc.* 1989;10:141-147.
51. Jacobs RL, Andrews CP, Coalson J. Organic antigen-induced interstitial lung disease: diagnosis and management. *Ann Allergy Asthma Immunol.* 2002;88:30-41.
52. Jacobs RL, Andrews CP, Jacobs FO. Hypersensitivity pneumonitis treated with an electrostatic dustfilter. *Ann Intern Med.* 1989;110:115-118.
53. Jacobs RL, Andrews CP. Hypersensitivity pneumonia-nonspecific interstitial pneumonia/fibrosis histopathologic presentation: a study in diagnosis and long-term management. *Ann Allergy Asthma Immunol.* 2003;90:265-270.
54. Pope AM, Patterson R, Burge H, editors. Indoor allergens. In: *Engineering Control Strategies*. Washington DC: National Academy Press; 1993:227.
55. New York City Department of Health, Bureau of Environmental & Occupational Disease Epidemiology. *Guidelines on Assessment and Remediation of Indoor Environments*. New York, NY: Department of Health, Bureau of Environmental & Occupational Disease Epidemiology; 1993.
56. Robbins CA, Swenson LJ, Neally ML, Gots RE, Kelman BJ. Health effects of mycotoxins in indoor air: a critical review. *Appl Occup Environ Hyg.* 2000;15:773-784.
57. Page EH, Trout DB. The role of *Stachybotrys* mycotoxin in building related illness. *Am Ind Hyg Assoc J.* 2001;62:644-648.
58. Hupakka DW, Buffington JR. Resolution of sick building syn-

- drome in a high-security facility. *Appl Occup Environ Hyg.* 2000;15:635-643.
59. Jarvis JQ, Morey PR. Allergic respiratory disease and fungal remediation in a subtropical climate. *Appl Occup Environ Hyg.* 2001;16:380-388.
60. Burge HA. Fungi: toxic killers or unavoidable nuisances? *Ann Allergy Asthma Immunol.* 2000;87(Suppl 3):52-56.
61. American Society of Heating, Refrigeration and Air-Condition Engineers Inc. *Thermal Environmental Conditions for Human Occupancy-ASHRAE Standard (ANSI/ASHRAE 55-1992).* At-

- lanta, GA: American Society of Heating, Refrigeration and Air-Condition Engineers Inc; 1992.
62. Martyny J, Glazer CS, Newman LS. Current concepts: respiratory protection. *N Engl J Med.* 2002;347:824-830.

Requests for reprints should be addressed to:
Jean Chapman, MD
1703 W Cape Rock Dr
Cape Girardeau, MO 63701-2610
E-mail: jchapman@swbellnet

Correspondence

To the Editor:

This letter is written in response to your February 2003 guest editorial entitled "Membership apathy." There is significant truth in Dr. Claffin's suggested reason for membership apathy. Caring for family and patients certainly plays a leading role in the lives of many of our colleagues. Dwindling remuneration for our services by third-party payers has caused many of our colleagues, especially those starting out in practice, to spend a great deal more time taking care of patients to make a reasonable living.

I agree with Dr. Claffin that those of our fellow physicians who have given much of their time and effort toward the establishment and maintenance of our professional societies may be nearing burnout. I do believe, however, that our past and present failure to unite on a professional level and in a professional manner has been a major contributor to membership apathy. When one peruses the many generic medical publications, one encounters primarily criticism, but seldom does one find, along with such criticism, proposals of solutions to the many problems we face.

Many of our younger colleagues consider generic medical societies to be "old boys' clubs" in which they cannot have a voice. Today's "what's in it for me" attitude causes others from joining and having a voice in their future.

It is not very often that one finds generic medical societies reaching out to attract new members, especially young physicians who have only recently entered the world of private practice either as principals or as employees, by offering worthwhile programs that help them understand the multitude of problems associated with practice management, billing, malpractice coverage, coding, Medicare, Medicaid, HIPAA, and the very basic economic elements of running, or participating in the running, of a practice. None of our medical schools prepares us for the real world of medicine, and, except for costly consultants, there are few avenues a new physician can pursue to learn the basics of running a practice.

So often the power politics of medicine become the regular topics of our generic societies, and the real needs of our colleagues are neglected. Apathy grows rapidly when the needs of the membership are not met.

I believe that it behooves all of us to take a good look at the mission of our societies. It may not be all that difficult to recognize that we can do much more to keep members and attract new ones. If we do, then perhaps we can attract young and energetic colleagues into our ranks, and burnout will not be a problem.

SURESH C. ANAND, MD
President
Maricopa County Medical Society
Phoenix, Arizona

CROSSING OVER TO THE DARK SIDE OF THE MOLD ISSUE: A DISSENTING VIEW

To the Editor:

Because of the sensational stories in the lay press concerning "black mold" published over the past few years, allergists and immunologists have both an opportunity and an obligation to help the concerned lay public sort out the junk from the junk science and to stem the tide of public hysteria. There is no doubt that mold may cause human disease and we all treat patients in whom mold allergy is a significant contributor to illness. But the issue of illness secondary to the mycotoxin from *Stachybotrys* is less well established. According to many experts, *Stachybotrys* has not been proven to cause verifiable disease by inhalation, including those patients whose immune systems are suppressed such as transplant recipients, patients on chemotherapy, and AIDS patients. As one examines publications that address the *Stachybotrys* mold issue, it is easy to understand that all is not black and white concerning issues relating to black mold. Harriet A. Burge, PhD (Harvard School of Public Health), states that extensive literature review "yielded many studies of the role of fungi in allergic disease, but none that systematically documented a role for mycotoxins or fungals volatiles."¹ Her review concluded that the primary consequence of fungal exposure is allergic disease and that evidence to support mycotoxin exposure as a causative agent for inhalation disease is "extremely weak." Abba I. Terr, MD, wrote a review in the same medical journal entitled "*Stachybotrys*: relevance to human disease."² Dr. Terr states in his review that "published reports fail to establish inhalation of *Stachybotrys* spores as a cause of human disease even in water-damaged buildings," although he does point out that ingestion of food prepared from *Stachybotrys*-contaminated grains may cause a toxic gastroenteritis. More recently, Jean Chapman, MD, published an excellent review of this subject; he concluded that "there is no compelling evidence that exposure levels expected in most mold-contaminated indoor environments are likely to result in measurable health effects."³

In the February 2003 issue of the *Annals*, Santilli and Rockwell⁴ claim, in the absence of scientific evidence, that our school children are in imminent danger from mold. We believe this study is misleading and may add to the public's confusion as to what is fact and what is fiction regarding mold. The absolute quantity of mold means little unless the individual is allergic to mold or has a hypersensitivity pneumonitis. Clearly, the presence of an "elevated" mold count does not necessarily define an unhealthy environment in the absence of proven allergy. This report is an uncontrolled retrospective speculation based on symptoms extracted from a questionnaire. Furthermore, the authors did not measure

mycotoxins or volatile organic compounds in the affected schools or in a parallel controlled environment. The fact that one of the schools described by Santilli and Rockwell was demolished is disturbing, and we would submit that the taxpayers of Connecticut might better use those funds for education. The accompanying guest editorial by Portnoy⁵ is equally disturbing. Portnoy states that we are "experiencing an epidemic of mold-related complaints . . . so the next time a patient arrives in your practice with a mold exposure, greet them enthusiastically." As allergists and as immunologists, we are frequently called upon by our communities; I urge allergists to become a voice of reason in the murky dark waters of black mold. Without sound science, many well meaning allergists might be tempted to go to the "dark side" of this issue and be sucked into the whirling vortex, contributing to unnecessary lawsuits.

If medical science does not justify the excessive public concern about this mold, then what group is driving this train? Perhaps the answer to that question can be found in an article written by Stephanie Francis Cahill, a writer with the *American Bar Association Journal*.⁶ In her article entitled "For some lawyers, mold is gold," she states that "[t]oxic troubles translate into millions of dollars" and that "the practice area is growing rapidly." She further adds, "In the past decade, attorneys have won millions of dollars in toxic mold verdicts in Texas, Delaware, and California." She goes on to note that claims for asbestos are fading into memory but that "with mold, it's naturally occurring and the supply is endless . . . claims involving adult onset asthma or cognitive functions such as short term memory loss can be lucrative. . . ." Well, perhaps we do know who is driving this train. The thoughtful allergist and immunologist may not wish to climb aboard this train until the engine is fueled by controlled scientific studies.

EMIL J. BARDANA, MD

JEAN A. CHAPMAN, MD

ERNEST N. CHARLESWORTH, MD

ROBERT L. JACOBS, MD

ABBA L. TERR, MD

REFERENCES

1. Burge HA. Fungi: toxic killers or unavoidable nuisances? *Ann Allergy Asthma Immunol.* 2001;87(Suppl 3):52-56.
2. Terr AI. *Stachybotrys*: relevance to human disease. *Ann Allergy Asthma Immunol.* 2001;87(Suppl 3):57-63.
3. Chapman JA. *Stachybotrys chartarum* (*chartarum* = *atra* = *alternans*) and other problems caused by allergenic fungi. *Allergy Asthma Proc.* 2003;24:1-7.
4. Santilli J, Rockwell W. Fungal contamination of elementary schools: a new environmental hazard. *Ann Allergy Asthma Immunol.* 2003;90:203-208.
5. Portnoy JM. Evaluation of indoor mold exposure is what allergists do best. *Ann Allergy Asthma Immunol.* 2003;90:175.
6. Cahill SF. For some lawyers, mold is gold. *Am Bar Assoc J.* 2001;87:22.

Response:

We read with interest the comments expressed by the authors of the above letter. We completely agree with their premise that sound data are necessary to dispel the myths and fallacies surrounding the mold issue. That is precisely why we performed this study. Although we feel that honest differences may exist among colleagues, it is imperative to point out that the February article was subjected to rigorous peer review and benefited from the constructive critiques provided by the reviewers.

Our research results published in the February issue of the *Annals* were gathered from observations made in patients seen in our private practice from 2 local schools in a state of disrepair. The atopic students and teachers in these schools were suffering from a variety of allergy-related symptoms that were linked to exposure to the high level of mold found in the schools.

Those hired to remediate the neglected schools found that extensive and costly repairs were needed, to the point where one of the towns involved decided it was more cost-effective to rebuild the school. Although the authors of the dissenting view may not consider indoor exposure to mold the major cause of any measurable health effects, we found that the 20% of the students and teachers affected by the mold were immeasurably relieved to see their health improve upon elimination of mold exposure.

The publicity surrounding the issue of "sick buildings," although detrimental at times, was helpful in this case by making parents more aware of increased mold-associated illness at the start of the school year, and this in turn has led to the earlier identification of mold contamination in a number of other public schools nationwide. The extent of mold contamination in public schools in Connecticut and across the country, however, has yet to be fully determined. In most of the schools we have been asked to examine, a wide range of health problems, from minor to very serious, could be attributed to indoor mold exposure. In some of these cases, the health issues cleared up once the buildings were remediated. In other more troublesome cases, however, the patient's health was not regained.

It is generally accepted that sensitivity to mold is a significant factor in the pathogenesis of allergic diseases. These diseases include allergic asthma, allergic rhinitis, allergic fungal sinusitis, bronchopulmonary mycoses, and hypersensitivity pneumonitis.¹ The cognizance of this association provided the rationale for the experimental design and research approach that we used in our study.

Current medical literature supports the detrimental role of indoor mold exposure on the health of students and teachers.²⁻⁴ Furthermore, governmental agencies have also recognized and commented upon the detrimental impact that exposure to high concentrations of mold and fungi can have on an individual's health.⁵⁻⁹

The overall indoor air quality of schools in the United States needs to be examined rigorously, particularly in areas

of the country where older schools exist. It is unfortunate that too many school districts have been forced by years of limited budgets to delay building maintenance and forgo repairs to maintain low teacher-to-student ratios. This in turn has sadly come to impact the health of many students and teachers. Allergist-immunologists can play an important role as patient advocates, protecting the health of children and teachers.

Mold exposure resulting from moisture damage has gone unchecked because of the poor condition of many schools and is contributing to this serious health issue in school-aged children and their teachers. Although there has been a dramatic increase in the awareness of the health problems caused by indoor mold exposure, as well as some increased resources to remediate the problems, there is a notable lack of standardization of testing indoor air quality. Standards are clearly needed to ensure acceptable air quality in schools. In a recent study by Bush and Portnoy,¹⁰ an unhealthy indoor environment was defined by a volumetric mold contamination count greater than 1,000 spores/m³.

It is not clear to us why the authors of the above letter chose to focus on the health impact of *Stachybotrys* exposure when it was not described in our article. Of course, some less-than-responsible members of the media have sensationalized the toxic mold story, and clearly the impact of *Stachybotrys* on human health has yet to be fully understood. However, this should not cause physicians to minimize the real suffering of atopic patients, generally thought to comprise 20% of the population, who are forced to spend their days in unhealthy indoor environments.

Physicians should not be hesitant to become public health advocates for fear of large lawsuits. The case reports described in our February article involved no class-action lawsuits or claims for multimillion dollar settlements. Rather, they reflect the results of communities working together to keep their children and teachers healthy.

Finally, we disagree with the authors in their attempts to trivialize the difficult decision made by the town of Fairfield to tear down one of their elementary schools. The taxpayers and town leaders in Fairfield are very concerned about both the health and the education of their children and did not make this decision based on sensationalized journalism. In fact, only after carefully weighing the cost/benefit consequences of all their options did they make this decision, one that they will be required to find funding for over the coming decades.

To restate the conclusions of the February article, "Due to the negative impact on health that indoor mold exposure has, particularly in atopic patients, schools should be routinely tested for fungal contamination. Total mold spore counts should be performed using volumetric air sampling such as the Allergenco MK-3 because testing air quality via semi-quantitative culture sampling alone does not give a true reflection of the extent of fungal contamination. Finally, the standard for a healthy indoor environment should be defined as having less than 1000 spores/m³."

We welcome the debate that our paper has engendered because it clearly demonstrates not only that further research is required in this critical area, but also that the allergist-immunologist has an important future role to play in resolving the many complex concerns surrounding mold issues in the school setting.

JOHN SANTILLI, MD
WILLIAM ROCKWELL, MD
Bridgeport, Connecticut

REFERENCES

1. Dziadzio L, Bush RK. Assessment and control of fungal allergens. *Curr Allergy Asthma Rep.* 2001;1:455-460.
2. Savilahti R, Uitti J, Laippala P, Husman T, Roto P. Respiratory morbidity among children following renovation of a water-damaged school. *Arch Environ Health.* 2000;55:405-410.
3. Savilahti R, Uitti J, Roto P, Laippala P, Husman T. Increased prevalence of atopy among children exposed to mold in a school building. *Allergy.* 2001;56:175-179.
4. Taskinen T, Hyvarinen A, Meklin T, Husman T, Nevalainen A, Korppi M. Asthma and respiratory infections in school children with special reference to moisture and mold problems in the school. *Acta Paediatr.* 1999;88:1373-1379.
5. Environmental Protection Agency. Mold remediation in schools and commercial buildings. Available at: www.epa.gov/iaq/molds/index.html.
6. Redd SC. *State of the Science on Molds and Human Health. Center for Disease Control and Prevention Statement for the Record before the Subcommittees on Oversight and Investigations and Housing and Community Opportunity.* July 18, 2002.
7. Occupational Safety and Health Administration, US Department of Labor. Indoor air quality. Available at: www.osha.gov/SLTC/indoorairquality/index.html.
8. Connecticut Education Association. Schoolhouse news. Available at: www.cea.org/NewsDesk/SHN/index.html.
9. The United States General Accounting Office. *Indoor Air Quality: School Facilities: America's Schools Report Differing Conditions.* GAO Report HEHS-96-103. Available at: www.gao.gov/.
10. Bush RK, Portnoy JM. The role and abatement of fungal allergens in allergic diseases. *J Allergy Clin Immunol.* 2001;107:S430-S440.

Response:

I respect the opinions voiced in the letter to the editor, and I agree with many of them. We do know that some individuals are sensitive to aeroallergens, including allergens from fungi. As allergists, we spend a great deal of effort identifying those patients and advising them to avoid exposure when possible.

Recently, our nation has been faced with a great deal of public concern over the potential health effects of mold exposure. This somehow is viewed differently than exposure to other allergens that have been proven to have serious adverse health effects, such as ragweed pollen. I believe that this is because although there is little we can do about ragweed exposure, and the health effects are fairly well understood. With mold, very little is known about the health effects. Even so, indoor exposure can be controlled and, most

importantly, in some cases someone can be blamed for the exposure. That is a prerequisite for any lawsuit. I doubt that the authors of the above letter would dismiss ragweed allergy if lawyers somehow figured how to file lawsuits over unmowed ragweed fields.

I appreciate the references to scientific articles cited above, but I must point out that absence of data does not prove that health effects are absent. The public is clearly concerned. To dismiss the mold issue simply as greed on the part of plaintiffs and their lawyers does our society a great disservice. If allergists do not embrace the issue in an intelligent manner and work with scared people, affected individuals may end up consulting the very mercenaries that the letter criticizes. People who believe that they have been harmed will go somewhere. The question is where will they go?

It remains my opinion that concerned individuals need to have access to knowledgeable allergy specialists who can address their fears. Allergists have had that role through the years with hidden food allergies, the yeast connection, and more recently with autism. So, I reiterate my opinion, "The next time a patient arrives in your practice with a mold exposure, greet them enthusiastically."¹ That does not mean that we should mislead them or inappropriately advocate for adverse health effects of mold, but we can at least listen to them, empathize with them, and keep an open mind. That is what we should do best.

JAY M. PORTNOY, MD
Section of Allergy/Asthma/Immunology
Children's Mercy Hospital and Clinic
Kansas City, Missouri

REFERENCE

1. Portnoy JM. Evaluation of indoor mold exposure is what allergists do best. *Ann Allergy Asthma Immunol.* 2003;90:175.

In her candid and thorough review¹ of the fourth edition of the *Manual of Allergy and Immunology*,² Dr. Susan Rudd Wynn approves of its penicillin desensitization protocol, but wonders if the chapters on connective tissue disease and immunohematology or transplantation immunology are useful for the practicing allergist. Dr. Wynn, a pediatric allergist/immunologist, notes that "few [patients with rheumatologic problems] turn to their allergists for treatment[, and] a good internist is much better qualified to treat these patients if a

rheumatologist is not available." Coincidentally, in the same issue of the *Annals*, Dr. Aaron Domm, an internal medicine resident, discusses a woman with adult-onset Still disease and anaphylaxis to infliximab, whose rheumatologist requested allergist/immunologist consultation for this drug reaction. He and I evaluated the patient and diagnosed possible IgG-mediated reactivity to infliximab. She subsequently received infliximab without complication. The moral of this story is that we allergists are also clinical immunologists by training. We may be consulted about patients with rheumatologic or other diseases treated with immunomodulatory agents. It behooves us to retain our familiarity with these entities, since we are uniquely qualified to diagnose and treat or prevent immunologic reactions to them, as well as to penicillin.

ANITA GEWURZ, MD

Departments of Immunology/Microbiology and Pediatrics
Rush Presbyterian St. Luke's Medical Center
Chicago, Illinois

REFERENCES

1. Wynn SR. Book review. *Ann Allergy Asthma Immunol.* 2003; 90:359.
2. Adelman DC, Casale TB, Corren J, editors. *Manual of Allergy and Immunology*. 4th ed. Baltimore, MD: Lippincott Williams Wilkins; 2002.
3. Domm A. A patient's reaction to infliximab. *Ann Allergy Asthma Immunol.* 2003;90:298-301.

Response:

I agree that the practicing allergist needs to have an understanding of rheumatology; my complaint about the *Manual of Allergy and Immunology* was not that rheumatology was included, but that the section seemed disproportionately large compared with the sections on allergy and asthma. We are, after all, board certified in both allergy and clinical immunology, and familiarity of all conditions with immune system dysfunction is required throughout our careers.

Drs. Gewurz and Domm's case report is an important addition to the allergy literature, but I think it reaffirms my argument; after all, the report was fundamentally about the diagnosis and management of drug allergy.

SUSAN RUDD WYNN, MD
Fort Worth Allergy and Asthma Associates
Fort Worth, Texas